REMARKS

Claims 1-14 and 44-70 are pending in this application for the Examiner's review and consideration. Claim 54 was amended to correct the claim numbering. No new matter has been added by this claim amendment so its entry at this time is warranted.

THE REJECTIONS UNDER 35 U.S.C. § 103(A)

The Rejection of Claim 1 as Being Obvious Over U.S. Patent No. 5,719,197 to Kanios *et al.*

Claim 1 was rejected under 35 U.S.C. § 103(a) as being obvious over U.S. patent no. 5,719,197 to Kanios *et al.* ("Kanios") for the reasons set forth on pages 2-4 of the Office Action. Specifically, the Examiner alleges that Kanios discloses a composition comprising a solvent, an active agent, and a carrier and that the solvents include fatty acids such as linoleic acid, the active agent can be fluoxetine, and that 2-hexyl decanoic acid is a lipophilic counterion. Therefore, the Examiner alleges it would have been obvious to employ fluoxetine, decanoic acid, and linoleic acid in a composition.

As the Examiner is aware, in order to render claims obvious under 35 U.S.C. § 103(a), the prior art must disclose or suggest every limitation of the claimed invention and provide the person of skill in the art with a reasonable expectation that the invention will work for its intended purpose. *KSR International Co. v. Teleflex Inc. et al.*, 127 S. Ct. 1727 at 1739-41 (2007).

Kanios does not disclose each and every feature of the invention recited in claim 1, suggest the invention, or provide a reasonable expectation of success. Without limitation as to other deficiencies in Kanios, the reference does not, at a minimum, disclose or suggest a composition that is "for oral administration or an injectable composition." Rather, Kanios discloses compositions that are for topical administration. The compositions disclosed in Kanios are not described as being suitable for oral administration or administration by injection. The requirements for a composition for topical administration are completely different from those for a composition for oral administration or administration by injection. For example, compositions for topical administration, unlike compositions for oral administration or administration by

injection, must be able to adhere to the skin or mucosa (*See*, Kanios, column 4, lines 62 to column 5, lines 5 and column 6, lines 23-27). Indeed, the compositions disclosed in Kanios include excipients, such as clays and bioadhesives, which allow the compositions to adhere to the skin and mucosa, that would not be suitable for inclusion in a composition for oral administration or administration by injection. Indeed, such compositions, because of the bioadhesive, are sticky and, therefore, could not be drawn into a syringe (*i.e.*, an "injectable composition, " *see*, specification, ¶ [0019]) or administered orally. Formulations for oral administration must be adequately absorbed when ingested and injectable formulations must be taken up into the system without causing undue tissue damage. Kanios is silent regarding these differences. There is simply no disclosure or suggestion in Kanios of a composition for oral administration or administration by injection or that the topical compositions disclosed therein could be modified so as to be suitable for oral administration or administration by injection. Moreover, even if Kanios did suggest that the formulations disclosed therein could be formulated for oral administration or administration by injection, which it does not, the reference does not provide the requisite reasonable expectation that such a composition, if formulated for oral administration or administration by injection, would successfully release the active compound over time. Indeed, the Examiner, by not rejecting claim 2, recognized that dependent claim 2, directed to an injectable composition, is patentable over Kanios.

Applicant notes that the Examiner states that

> A recitation of intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claim.

(*See*, Office Action, page 3). The recitation in claim 1 "to form a composition for oral administration or an injectable composition" is not an intended use but a characteristic of the claimed composition (they can be drawn into a syringe and injected or administered orally, *i.e.*, swallowed), characteristics that clearly distinguish the claimed composition from the compositions disclosed in Kanios (*i.e.*, adhesive topical compositions). Defining a part of an invention by functional language is permitted (Manual of Patent Examining Procedure ("MPEP") ¶ 2173.05(g)). "Functional language does not, in and of itself, render a claim

improper" (MPEP ¶ 2173.05(g), citing *In re Swinehart*, 439 F.2d, 210, (CCPA 1971)) and "the limitation used to define a radical on a chemical compound as 'incapable of forming a dye with said oxidizing developing agent' although functional, was perfectly acceptable because it set definite boundaries on the patent protection sought" (MPEP ¶ 2173.05(g), citing *In re Barr*, 444 F.2d 588 (CCPA 1971)). The recitation in claim 1 "to form a composition for oral administration or an injectable composition" clearly distinguished the claimed composition from that disclosed in Kanios and, as discussed above, there is absolutely no recognition in Kanios of a composition for oral administration or administration by injection or that the topical compositions disclosed therein could be modified so as to be suitable for oral administration or administration by injection.

The rejection of claim 1 as being obvious over Kanios is the impermissible use of hindsight to reconstruct Applicants' invention. The Examiner has used Applicants' invention as a blueprint to combine selected parts of Kanios, when there is no motivation to do so, to arrive at Applicants' invention. It is well settled that hindsight cannot be used to reject a claim as obvious. *In re Sernaker,* 702 F.2d 989, 994 (Fed. Cir. 1983); *In re Rinehart, 531* F.2d 1048 (CCPA 1976); *In re Imperato,* 486 F.2d 585 (CCPA 1973); *In re Adams,* 356 F.2d 998 (CCPA 1966); *In re Anita Dembiczak,* 75 F.3d 994, 999 (Fed. Cir. 1999); *C.R. Bard Inc. v. M3 Systems, Inc.,* 157 F.3d 1340, 1352 (Fed. Cir. 1998) citing *Fromson v. Advance Offset Plate, Inc.,* 755 F.2d 1549, 1556 (Fed. Cir. 1985) (holding the prior art must suggest to one of ordinary skill in the art the desirability of the claimed combination).

For example, the Examiner cites Kanios as disclosing linoleic acid as a water immiscible solvent. Linoleic acid, however, is selected from a long list of useful solvents, most of which are water miscible (*See*, Kanios, column 4, lines 3-11). There is, however, no disclosure or suggestion to select a solvent that is a water immiscible solvent, as required by claim 1.

Similarly, the Examiner selects fluoxetine from a laundry list of pharmacologically active compounds that spans more than 19 columns of the patent. There is, however, no disclosure or suggestion to select a pharmacologically active compound that is capable of forming a salt with a lipophilic counterion. The Examiner further selects 2-hexyldecanoic acid from the laundry list of pharmacologically active compounds disclosed in Kanios as disclosing a lipophilic counterion.

Kanios, however, merely discloses that fluoxetine and 2-hexyldecanoic acid are pharmacologically active compounds that can be used in the topical compositions disclosed therein. There is, however, no motivation provided in Kanios to combine a lipohilic counterion (such as 2-hexyldecanoic acid) with a pharmacologically active compound (such as fluoxetine) to provide a salt, much less that the resulting salt should be combined with a water immiscible solvent, to form a composition for oral administration or an injectable composition. Applicants respectfully submit that Kanios can only be construed to render claim 1 obvious by the impermissible use of hindsight reconstruction.

For the reasons set forth above, Applicants respectfully request that the rejection of claim 1 under 35 U.S.C. § 103(a) as being obvious over Kanios be reconsidered and withdrawn.

The Rejection of Claims 1, 44, 45-48, 50, 51, 54, and 55-13 Under 35 U.S.C. § 103(a) as Being Obvious Over U.S. Patent No. 7,011,846 to Shojaei *et al.*

Claims 1, 44, 45-48, 50, 51, 54, and 55-13 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. patent no. 7,011,846 ("Shojaei") for the reasons set forth on pages 6-7 of the Office Action. Specifically, the Examiner alleges that Shojaei teaches a composition for oral administration comprising an active compound such as fluoxetine, a lipophilic counterion (decanoic acid), and a water immiscible solvent (castor oil). Applicants respectfully traverse.

Shojaei discloses an oral capsule containing non-aqueous solubilizers with increased physical stability (*See*, Shojaei, column 1, lines 41-43). According to Shojaei non-aqueous solubilizers can adversely effect capsule integrity (*Id.* at column 1, lines 14-34). By including a capsule stabilizing agent, stability of the capsule is improved (*Id.* at column 1, lines 49-54). Capsule stabilizing agents include fatty esters of glycerol, fatty esters of polyethylene glycol, fatty esters of propylene glycol, fatty acids, and mixtures thereof (*Id.* at column 2, lines 11-14). Shojaei simply describes a method for stabilizing capsules.

Shojaei, however, does not disclose each and every feature of the invention recited in independent claims 1 and 44, suggest the invention, or provide a reasonable expectation of success. Shojaei simply discloses various components can minimize decomposition of a capsule from exposure to a non-aqueous solubilizer such as 2-pyrrolidone and N-C_{1-4} alkylpyrrolidones. There is, however, no disclosure to form a salt between a pharmacologically active compound

and a lipophilic counterion or to combine the resulting salt with a water immiscible solvent. The Examiner asserts that Shojaei discloses fluoxetine as a pharmacologically active compound. Fluoxetine, however, is simply included in Shojaei as part of a long laundry list of active compounds (*Id.* at column 4, line 66 to column 7, line 28). The Examiner then cites Table 1 of Shojaei as disclosing decanoic acid as a lipophilic counterion. Table 1, however, merely shows that decanoic acid is a suitable stabilizer for N-methyl-2-pyrrolidone ("NMP"). There is, however, no disclosure or suggestion in Shojaei that would motivate one of ordinary skill in the art to select, from the laundry list of pharmacologically active compounds disclosed therein, a pharmacologically active compound that can form a salt with a lipophilic counterion, to form a salt between the pharmacologically active compound and a lipophilic counterion, and to then combine the resulting salt with a water immiscible solvent. Indeed, there is no disclosure in Shojaei of using a water immiscible solvent. The Examiner asserts that Table 1 of Shojaei discloses castor oil as a water immiscible solvent. The capsules used in Table 1, however, are filled with NMP (*Id.* at column 8, line 56 to column 9, line 1), which is a water *miscible* solvent (not water immiscible, as required by claim 1). The castor oil is merely used as a stabilizing agent. Moreover, Table 1 shows that castor oil is *not* a suitable stabilizer for NMP. Thus, if anything, Shojaei teaches away from using castor oil.

Moreover, even if Shojaei did provide the requisite motivation, which it does not for the reasons stated above, the reference provides no reasonable expectation that such a composition would be effective as a composition for oral administration or an injectable composition that releases the active compound over time when administered to a mammal, as recited in independent claims 1 and 44. Applicants respectfully submit that the rejection of the claims as obvious over Shojaei is the impermissible use of hindsight in an attempt to reconstruct Applicants' invention. The Examiner is selectively picking and choosing various parts of the broad disclosure of Shojaei, without any motivation to do so, to reconstruct Applicants' invention. As discussed above, such hindsight reconstruction is impermissible.

For the reasons set forth above, Applicants respectfully request that the rejection of claims 1, 44, 45-48, 50, 51, 54, and 55-13 under 35 U.S.C. § 103(a) as being obvious over Shojaei be reconsidered and withdrawn.

The Rejection of Claims 1-5, 11, 12, 44, 45-48, 50, 51, 54, 55, 58-61, 67, and 68 Under 35 U.S.C. § 103(a) as Being Obvious Over U.S. Patent No. 6,174,540 to Williams *et al.*

Claims 1-5, 11, 12, 44, 45-48, 50, 51, 54, 55, 58-61, 67, and 68 were rejected under 35 U.S.C. § 103(a) as being obvious over U.S. patent no. 6,174,540 ("Williams") for the reasons set forth on pages 7-8 of the Office Action. Specifically, the Examiner alleges that Williams teaches an injectable formulation comprising an active agent, such as an antibiotic, and a water immiscible solvent, hydrogenated castor oil, and capric acid. Applicants respectfully traverse.

Williams discloses a long acting injectable formulation that includes a therapeutic agent, hydrogenated castor oil, and a hydrophobic carrier (*See*, Williams, column 3, lines 46-59).

Williams, however, like Shojaei, does not disclose each and every feature of the invention recited in independent claims 1 and 44. Specifically, contrary to the Examiner's assertions, Williams does not disclose or suggest a lipophilic counterion. The Examiner asserts that the abstract discloses a formulation that includes capric acid. The abstract, however, does *not* disclose a formulation that includes capric acid. Rather, the abstract discloses "propyl discaprylates/dicaprates, caprylic/capric acid triglycerides," which are *esters* of caprylic acid and capric acid. Being *esters* of caprylic acid and capric acid, rather than the free acid, they are not capable of forming a salt with a pharmacologically active compound and, thus, are not a lipophilic counterion. Accordingly, there is no disclosure or suggestion in Williams of a salt formed between a pharmacologically active compound and a lipophilic counterion, much less to combine this salt with a water immiscible solvent. Moreover, there is nothing in Williams that would motivate one of ordinary skill in the art to form a salt between a pharmacologically active compound and a lipophilic counterion and to then combine the resulting salt with a water immiscible solvent.

For the reasons set forth above, Applicants respectfully request that the rejection of claims 1-5, 11, 12, 44, 45-48, 50, 51, 54, 55, 58-61, 67, and 68 under 35 U.S.C. § 103(a) as being obvious over Williams be reconsidered and withdrawn.

The Rejection of Claims 1-8,11,12, 14, 44-51, 54, 55, 57-64, 67, 68, and 70 Under 35 U.S.C. § 103(a) as Being Obvious Over U.S. Patent No. 6,309,663 to Patel *et al.*

Claims 1-8, 11, 12, 14, 44-51, 54, 55, 57-64, 67, 68, and 70 were rejected under 35

U.S.C. § 103(a) as being obvious over U.S. patent no. 6,309,663 ("Patel") for the reasons set forth on page 8-9 of the Office Action. Specifically, the Examiner asserts that Patel discloses a pharmaceutical composition for oral or parenteral use comprising an active agent, such as gentamycin or fluoxetine that is combined with a hydrophobic surfactant (water immiscible solvent), such as castor oil, palm kernel oil, and corn oil, and ionizable surfactants that are in their ionized form, such as oleic acid, capric acid, linoleic acid, and lauric acid. Applicants respectfully traverse.

Patel discloses a triglyceride free pharmaceutical system having a dosage form of an absorption enhancing composition comprising at least two surfactants, at least one of which is hydrophilic, and a hydrophobic therapeutic agent (*See*, Patel, column 4, lines 1-5).

Similar to the other references, Patel does not disclose each and every feature of the invention recited in independent claims 1 and 44, suggest the invention, or provide a reasonable expectation of success. Patel discloses an absorption enhancing formulation. Patel, however, does not disclose or suggest forming a salt between a pharmacologically active compound and a lipophilic counterion or to combine the resulting salt with a water immiscible solvent. The Examiner asserts that Patel discloses gentamycin and fluoxetine as a pharmacologically active compound. Each of these compounds, however, is simply included as part of a long laundry list of active compounds (*Id.* at column 29, line 41 to column 32, line 18). Similarly, the Examiner asserts that Patel discloses ionizable surfactants that are in their ionized form, such as oleic acid, capric acid, linoleic acid, and lauric acid. Again the disclosure of these surfactants is part of a long laundry list of surfactants spanning over 10 pages of the patent (*Id.* at column 6, line 55 to column 29 line 5). There is, however, no disclosure or suggestion in Patel that would motivate one of ordinary skill in the art to select, from the long laundry list of active compounds recited therein, a pharmacologically active compound that can form a salt with a lipophilic counterion or to select, from the long laundry list of surfactants disclosed therein, a surfactant that is a lipophilic counterion, to then form a salt between the pharmacologically active compound and the lipophilic counterion, and then combine the resulting salt with a water immiscible solvent. Moreover, Patel provides no reasonable expectation that such a composition would successfully release the active compound over time.

Again, Applicants respectfully submit that the Examiner's rejection of the claims is the impermissible use of hindsight in an attempt to reconstruct Applicants' invention. The Examiner is selectively picking and choosing various parts of the broad disclosure of Patel, absent a motivation to do so, to reconstruct Applicants' invention. As discussed above, such hindsight reconstruction is impermissible.

For the reasons set forth above, Applicants respectfully request that the rejection of claims 1-8,11,12, 14, 44-51, 54, 55, 57-64, 67, 68, and 70 under 35 U.S.C. § 103(a) as being obvious over Patel be reconsidered and withdrawn.

THE REJECTION OF CLAIMS 1-14 AND 45-57 UNDER 35 U.S.C. § 112, SECOND PARAGRAPH

Claims 1-14 and 45-57 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for the reasons set forth on page 5 of the Office Action. Specifically, the Examiner asserted that the phrase "over time" in claim 1 is indefinite because "it is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention" (Office Action, page 5). Applicants respectfully traverse. The specification clearly defines what is meant by the phrase "over time." The specification clearly recites

> By releasing the pharmacologically active compound "over time" is meant that the active compound is present in the blood or treated tissue of the mammal at pharmaceutically effective amounts for at least 2 days after administration.

(*See*, Specification, ¶ [0016]). The specification also clearly defines the term "pharmaceutically effective amount" (*Id.* at ¶ [0016]). Accordingly, Applicants respectfully submit that, contrary to the Examiner's assertion, the specification does "provide a standard for ascertaining the requisite degree."

The Examiner also asserted that claim 55 is indefinite because it recites "the composition of claim 53 wherein the pharmaceutically acceptable water immiscible solvent is selected from the group consisting of one or more of" and there is "insufficient antecedent basis for this limitation in the claim because there is not a water immiscible solvent recited in claim 53." Applicant notes that dependent claim 55 depends ultimately from claim 1 (via dependence on

claims 53, 52, and 45). Independent claim 1 recites the limitation of "a water immiscible solvent." A dependent claim includes all the limitations of the claims from which it depends. Accordingly, there is sufficient antecedent basis for the limitation of "a water immiscible solvent" in dependent claim 55.

For the reasons set forth above, Applicants respectfully request that the rejection of claims 1-14 and 45-57 under 35 U.S.C. § 112, second paragraph, be reconsidered and withdrawn.

DOUBLE PATENTING

Claims 1-14 and 44-70 were provisionally rejected on the grounds of non-statutory obviousness-type double patenting as being unpatentable over claims 65-138 of co-pending application serial no. 11/088,922 ("the '992 application") for the reasons set forth on pages 10-11 of the Office Action. Specifically, the Examiner alleges that claims of the present application are not patentably distinct from the claims of the '992 application because the instant and conflicting claims recite substantially the same subject matter differing only in the description of the particular components claimed.

Applicants note that the rejection is provisional. Accordingly, once all rejections of the claims over prior art have been addressed, Applicants will submit a Terminal Disclaimer disclaiming the term of any patent that should issue from the above-identified application that would extend beyond the term of the '992 application.

CONCLUSIONS

It is respectfully submitted that all claims are now in condition for allowance, early notice of which would be appreciated. Should the Examiner disagree, Applicants respectfully request a telephonic or in-person interview with the undersigned attorney to discuss any remaining issues and to expedite eventual allowance of the claims.

No fee is believed to be due for this submission. Should any additional fees be required, please charge the required fees to Kenyon & Kenyon deposit account no. 11-0600.

Respectfully submitted,

Date: July 23, 2007

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